One Year Post Exclusivity Adverse Event Review: Ofloxacin Ophthalmic

Pediatric Advisory Committee Meeting
September 15, 2004

Hari Cheryl Sachs, MD, FAAP
Medical Officer
Division of Pediatric Drug Development
Center for Drug Evaluation and Research
Food and Drug Administration

Background Drug Information

- **Moiety:** Ocuflox® (ofloxacin)
- **Therapeutic Category:** ophthalmic anti-infective
- **Sponsor:** Allergan
- **Adult and Pediatric Indications:** treatment of conjunctivitis and corneal ulcers for susceptible bacteria in patients > 1 year
- **Dosage:** 1-2 drops at frequent intervals depending on condition
- **Original Market Approval:** July 30, 1993
- **Pediatric Exclusivity Granted:** March 12, 2003

Drug Use Trends in Outpatient Settings: Ofloxacin

- Comprises 12 % of total 11.6 million prescriptions for medium and broad spectrum ophthalmics during exclusivity period (decreased from 20 % prior two years)[1]
- While total dispensed prescriptions have decreased from 2.2 million to 1.4 million during April 2003- March 2004[1], pediatric usage has remained steady.[2]
- Pediatric patients (ages 1-16) accounted for approximately one third of total U.S. prescriptions of Ocuflox® between April 2003 – March 2004 (460,752).[1,2*]

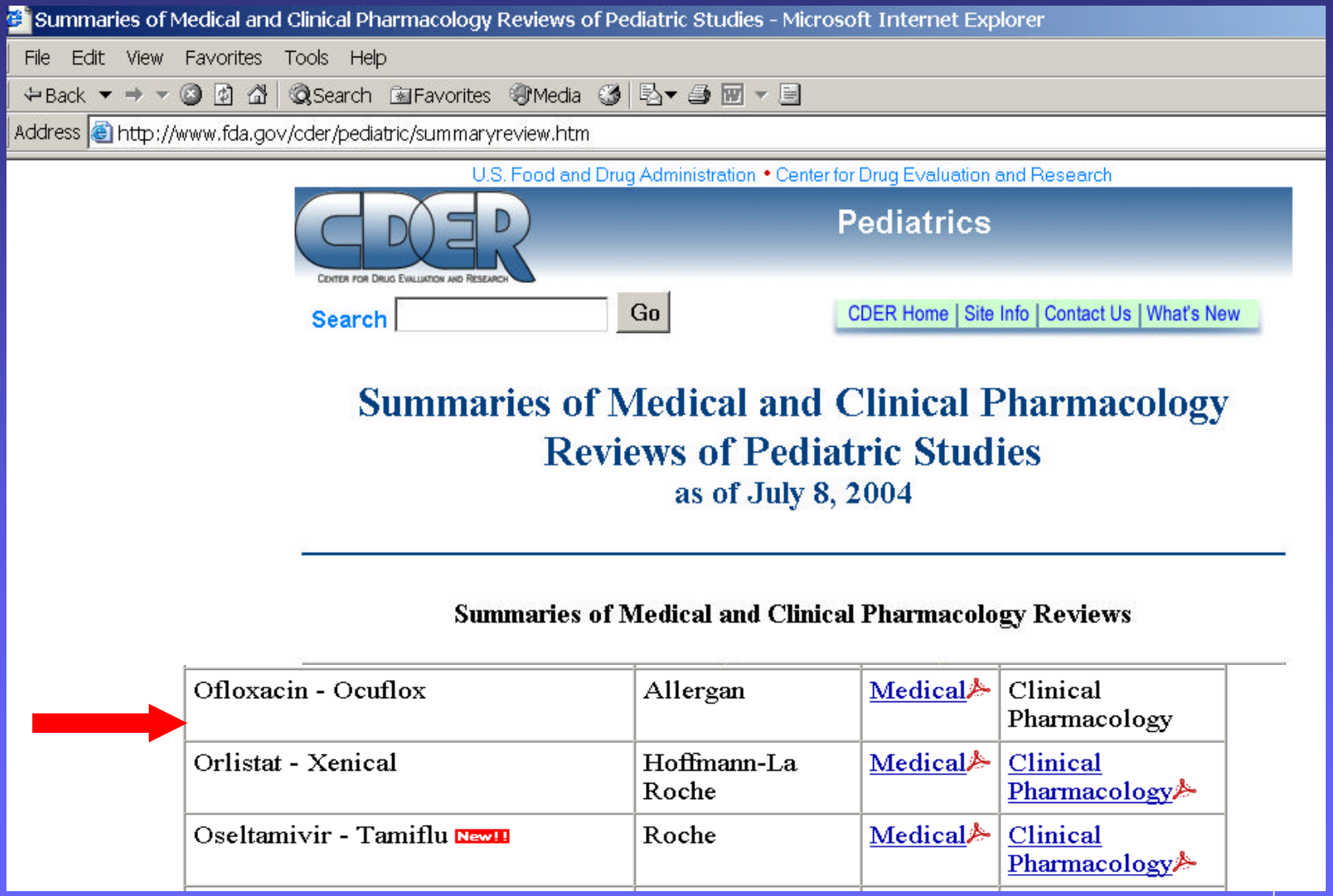
[1]IMS Health, National Prescription Audit *Plus*? , On-Line, Apr 2001 – Mar 2004, Data Extracted May 2004
[2]AdvancePCS? Dimension Rx, On-Line, Apr 2002 – Mar 2004, Data Extracted May 2004
*Calculation based on application of proportions of pediatric ofloxacin prescriptions in AdvancePCS? to IMS Health, National Prescription Audit *Plus*? to estimate number of ofloxacin prescriptions dispensed nationwide to pediatric population

Drug Use Trends in Outpatient Settings: Ofloxacin

- Prescribers: Ophthalmologists (39 %) and Pediatricians (26 %)[1]
- Pediatric Diagnosis: Conjunctivitis (77 % drug mentions)[2]

[1]IMS Health, National Prescription Audit *Plus*? , On-Line , Apr 2001- Mar 2004, Data Extracted May 2004
[2]IMS Health, National Disease and Therapeutic Index? , CD-Rom, Apr 2001 - Mar 2004, Data Extracted May 2004

http://www.fda.gov/cder/pediatric/Summaryreview.htm



Pediatric Exclusivity Studies: Ofloxacin

- One week, multicenter, randomized, double blind, parallel group trial comparing ofloxacin 0.3 % to trimethoprim sulfate/polymyxin b in neonates.
  - Cure rate= 60 % (vehicle 70 %)
  - Safety comparable to prior studies
  - Unable to determine from data submitted why clinical cure rate was low
- No label change resulted

Relevant Safety Labeling

- Pregnancy Category C
- Pediatric Use: Arthropathy in immature animals from oral (not topical) quinolones
- Warning: Hypersensitivity/anaphylaxis
- Adverse Reactions:
  - Transient ocular burning or discomfort
  - Other local symptoms (stinging, redness itching, chemical conjunctivitis/keratitis, edema, tearing, dryness and eye pain)
  - Visual changes- photophobia, blurred vision
  - Rare dizziness and nausea

Adverse Event Reports Since Market Approval: Ofloxacin
July 1993 – April 2004

- Total number of reports, all ages:
  - 66 reports (50 US)
    - 18 serious (7 US)
    - 4 deaths (0 US)
- Pediatric reports:
  - 3 reports (2 US)
    - 1 serious (0 US)
    - 0 deaths

Raw counts (US reports are in parenthesis)- includes duplicates

Adverse Events during the One-Year Post-Exclusivity Period: Ofloxacin
March 2003 – April 2004

- Adult (2)
  - Deafness neurosensory (1)
  - Hearing loss (1)
- Pediatric (1)
  - Corneal deposits (1)
- All events are unlabeled

Pediatric Adverse Event (n=1)

6 year old male

- Treatment for vernal conjunctivitis with topical ofloxacin ointment and drops TID for 3 weeks, along with prednisolone
- Developed dense, white, sharply demarcated corneal deposits treated with corneal scraping

Summary

- With one event, no meaningful conclusion can be drawn.
- This completes the one-year post-exclusivity adverse event monitoring as mandated by BPCA.
- FDA will continue its routine monitoring of adverse events for this drug.